

In re Application of:
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Application No.: 10/564,580
Filing Date: December 20, 2007
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PATENT
Attorney Docket No.: JHU2010-1

Amendments to the Claims:

Please amend claims 1, 3, 12, and 14, as provided below in the Listing of Claims.

Please cancel claims 4 and 15.

Please add new claims 68-73.

The listing of claims will replace all prior version, and listings, of claims in the application:

Listing of Claims:

1. (Currently Amended) A method of reducing or inhibiting ~~proliferation~~ metastasis of cells of a metastatic digestive tract tumor characterized by abnormally elevated Hedgehog (Hh) pathway activity, comprising contacting the cells with at least one Hh pathway antagonist, thereby reducing or inhibiting proliferation of the cells of the digestive tract tumor, wherein the cells are pancreatic cancer cells, stomach cancer cells, esophagus cancer cells, or biliary tract cancer cells.

2. (Original) The method of claim 1, wherein the digestive tract tumor is a malignant tumor.

3. (Currently Amended) The method of claim 2, wherein the cells are pancreatic cancer cells, ~~stomach cancer cells, esophagus cancer cells, or biliary tract cancer cells.~~

4. (Canceled)

5. (Original) The method of claim 1, wherein the abnormally elevated Hh pathway activity comprises abnormally elevated ligand stimulated Hh pathway activity.

6. (Original) The method of claim 5, wherein the ligand comprises Sonic hedgehog (SHH) or Indian hedgehog (IHH).

7. (Original) The method of claim 1, wherein the Hh pathway antagonist comprises a peptide, a polynucleotide, a peptidomimetic, or a small organic molecule.

8. (Original) The method of claim 1, wherein the Hh pathway antagonist comprises an anti-Hh antibody.

9. (Original) The method of claim 6, wherein the anti-Hh antibody comprises an anti-SHH antibody, an anti-IHH antibody, or an anti-SHH antibody and an anti-IHH antibody.

10. (Original) The method of claim 1, wherein the Hh pathway antagonist comprises a steroidal alkaloid or a derivative thereof.

11. (Original) The method of claim 10, wherein Hh pathway antagonist comprises cyclopamine.

12. (Currently Amended) A method of ameliorating a metastatic digestive tract tumor comprising cells characterized by abnormally elevated Hedgehog (Hh) pathway activity in a subject, comprising administering to the subject an Hh pathway antagonist, whereby the Hh pathway antagonist contacts cells of the tumor in the subject, wherein the cells are pancreatic cancer cells, stomach cancer cells, esophagus cancer cells, or biliary tract cancer cells, thereby ameliorating the digestive tract tumor in the subject.

13. (Original) The method of claim 12, wherein the digestive tract tumor is a malignant tumor.

14. (Currently Amended) The method of claim 13, wherein the cells are pancreatic cancer cells, ~~stomach cancer cells, esophagus cancer cells, or biliary tract cancer cells.~~

15. (Canceled)

16. (Original) The method of claim 12, wherein the abnormally elevated Hh pathway activity comprises abnormally elevated ligand stimulated Hh pathway activity.

17. (Original) The method of claim 12, wherein the Hh pathway antagonist is administered orally.

18. (Original) The method of claim 12, wherein the Hh pathway antagonist comprises a peptide, a polynucleotide, a peptidomimetic, or a small organic molecule.

19. (Original) The method of claim 12, wherein the Hh pathway antagonist comprises an antibody.

20. (Original) The method of claim 19, wherein the antibody comprises an anti-Sonic hedgehog antibody, an anti-Indian hedgehog antibody, or a combination thereof.

21. (Original) The method of claim 12, wherein the Hh pathway antagonist comprises a steroidal alkaloid or a derivative thereof.

22. (Original) The method of claim 21, wherein Hh pathway antagonist comprises cyclopamine.

23. (Withdrawn) A method of identifying a digestive tract tumor of a subject amenable to treatment with a Hedgehog (Hh) pathway antagonist, comprising detecting abnormally

elevated Hh pathway activity in a sample of cells of the digestive tract tumor of the subject as compared to Hh pathway activity in corresponding normal cells, thereby identifying a digestive tract tumor of a subject amenable to treatment with an Hh pathway antagonist.

24. (Withdrawn) The method of claim 23, wherein the abnormally elevated Hh pathway activity comprises ligand stimulated Hh pathway activity.

25. (Withdrawn) The method of claim 23, comprising detecting abnormally elevated expression of at least one Hh pathway polypeptide.

26. (Withdrawn) The method of claim 25, wherein the Hh pathway polypeptide comprises an Hh ligand, an Hh ligand receptor, or a transcription factor.

27. (Withdrawn) The method of claim 26, wherein the Hh ligand comprises Sonic hedgehog (SHH), Indian hedgehog (IHH), or SHH and IHH.

28. (Withdrawn) The method of claim 26, wherein the Hh ligand receptor comprises Patched.

29. (Withdrawn) The method of claim 26, wherein the transcription factor comprises a GLI-1 transcription factor.

30. (Withdrawn) The method of claim 25, which comprises detecting elevated levels of a polynucleotide encoding the Hh pathway polypeptide.

31. (Withdrawn) The method of claim 30, wherein the polynucleotide comprises RNA.

32. (Withdrawn) The method of claim 31, which comprises performing a reverse transcription-polymerase chain reaction.

33. (Withdrawn) The method of claim 25, which comprises detecting elevated levels of the Hh pathway polypeptide.

34. (Withdrawn) The method of claim 33, which comprises performing an immunoassay.

35. (Withdrawn) The method of claim 23, comprising detecting abnormally elevated activity of the Hh pathway polypeptide.

36. (Withdrawn) The method of claim 35, wherein the Hh pathway polypeptide comprises a transcription factor.

37. (Withdrawn) The method of claim 46, which comprises detecting increased binding activity of the transcription factor to a cognate transcription factor regulatory element.

38. (Withdrawn) The method of claim 36, which comprises detecting increased expression of a reporter gene comprising a cognate transcription factor regulatory element.

39. (Withdrawn) The method of claim 25, which comprises detecting altered expression of a transcriptional target of the Hh pathway.

40. (Withdrawn) The method of claim 39, wherein the transcriptional target comprises a nestin gene or a BMI-1 gene.

41. (Withdrawn) The method of claim 39, which comprises detecting increased expression of a gene that is positively regulated by GLI-1 or GLI-2.

42. (Withdrawn) The method of claim 39, which comprises detecting decreased expression of gene that is negatively regulated by GLI-3.

43. (Withdrawn) The method of claim 23, comprising detecting abnormally decreased expression of at least one Hh pathway polypeptide.

44. (Withdrawn) The method of claim 43, wherein the Hh pathway polypeptide comprises a Gli-3 transcription factor.

45. (Withdrawn) The method of claim 23, wherein the sample comprises a biopsy sample obtained from the subject.

46. (Withdrawn) The method of claim 23, further comprising contacting cells of the sample with at least one Hh pathway antagonist, and detecting a decrease in Hh pathway activity in the cells following said contact, thereby confirming that the digestive tract tumor is amenable to treatment with an Hh pathway antagonist.

47. (Withdrawn) A method of identifying an agent useful for treating a digestive tract tumor having abnormally elevated Hedgehog (Hh) pathway activity, comprising contacting a sample of cells of a digestive tract tumor with at least one test agent, wherein a decrease in Hh pathway activity in the presence of the test agent as compared to Hh pathway activity in the absence of the test agent identifies the agent as useful for treating the digestive tract tumor.

48. (Withdrawn) The method of claim 47, wherein the abnormally elevated Hh pathway activity comprises abnormally elevated ligand stimulated Hh pathway activity.

49. (Withdrawn) The method of claim 47, wherein the agent comprises a peptide, a polynucleotide, a peptidomimetic, or a small organic molecule.

50. (Withdrawn) The method of claim 47, wherein the agent comprises an Hh pathway antagonist.

51. (Withdrawn) The method of claim 50, wherein the Hh pathway antagonist comprises an antibody.

52. (Withdrawn) The method of claim 51, wherein the antibody comprises an anti-Sonic hedgehog antibody, an anti-Indian hedgehog antibody, or a combination thereof.

53. (Withdrawn) The method of claim 50, wherein the Hh pathway antagonist comprises a steroidal alkaloid or a derivative thereof.

54. (Withdrawn) The method of claim 53, wherein Hh pathway antagonist comprises cyclopamine.

55. (Withdrawn) The method of claim 50, wherein the Hh pathway antagonist comprises a Smoothened antagonist.

56. (Withdrawn) The method of claim 47, wherein the sample of cells of the digestive tract tumor is obtained from a subject having the digestive tract tumor.

57. (Withdrawn) The method of claim 56, wherein the sample of cells is obtained by biopsy.

58. (Withdrawn) The method of claim 56, wherein the digestive tract tumor comprises a malignant tumor.

59. (Withdrawn) The method of claim 58, wherein the cells are pancreatic cancer cells, stomach cancer cells, esophagus cancer cells, or biliary tract cancer cells.

60. (Withdrawn) The method of claim 58, wherein the cells are colon cancer cells.

61. (Withdrawn) The method of claim 47, which said contacting comprises contacting the sample of cells in culture.

62. (Withdrawn) The method of claim 47, which is performed in a high throughput format.

63. (Withdrawn) The method of claim 62, comprising contacting samples of cells of a plurality of samples with at least one test agent.

64. (Withdrawn) The method of claim 63, wherein samples of cells of the plurality are obtained from a single subject.

65. (Withdrawn) The method of claim 64, comprising contacting different samples of cells of the plurality with same amounts of a test agent, with different amounts of a test agent, with same amounts of different test agents, with different amounts of different test agents, or a combination thereof.

66. (Withdrawn) The method of claim 63, wherein samples of cells of the plurality are obtained from different subjects.

67. (Withdrawn) The method of claim 46, comprising contacting the cells with at least two test agents.

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68. (New) The method of claim 2, wherein the cells are stomach cancer cells.
69. (New) The method of claim 2, wherein the cells are esophagus cancer cells.
70. (New) The method of claim 2, wherein the cells are biliary tract cancer cells.
71. (New) The method of claim 12, wherein the cells are stomach cancer cells.
72. (New) The method of claim 12, wherein the cells are esophagus cancer cells.
73. (New) The method of claim 12, wherein the cells are biliary tract cancer cells.